REMARKS

This application was filed with claims 1-20. Claims 1-20 were canceled by previous amendment. Claims 24 and 35 have been canceled herein, without prejudice. No new claims have been added herein. Therefore, claims 21-23, 25-34, and 36-45 are pending. Claims 23, 28-34, 36-38, and 44 have been withdrawn from consideration by the Examiner. Claims 21-22, 33, and 42-43 have been amended herein.

Claim Amendments

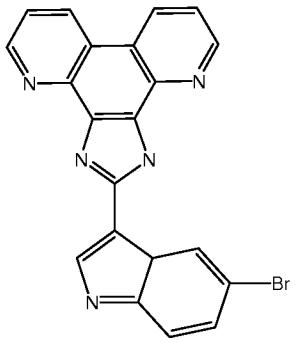
Claim 21 has been amended to remove "N" from the choice of substituents in the definitions of x and x' and to add "hydroxyl" back into the list of substituents defined for R4. No new matter has been added. Support for these amendments is found throughout the specification as filed, for example, in the examples of the present application.

For consistency with the amendments to claim 21, claims 22, 33 and 42 have also been amended to add "hydroxyl" back into the list of substituents defined for R4.

Rejection under 35 U.S.C. §102

The Office Action has maintained the rejection of claims 21, 22, 24 to 27, 39 to 43 and 45 under 35 U.S.C. §102(b) as being anticipated by Dora *et al.*, "Synthesis of Some Fused 2-Arylimidazoles and their Derivatives", J. Indian Chem. Soc. LVI, 1979, p. 620-624 ("Dora"). The Examiner stated that Applicants' arguments filed on July 8, 2010, have been fully considered but are not persuasive.

Specifically, the Office Action alleges that Dora teaches the following compound and that this compound is the result of reacting a compound of formula IV as described on page 620 of Dora with 5-bromo indole-3-carboxylic aldehyde (identified as "i" at the bottom of Table 1) in a simple condensation reaction.



As a preliminary matter, Applicants note that the compound identified by the Office Action (and noted above) does not fall within the scope of currently pending claims 25, 26, 39, 40 to 43 or 45, as these claims either specifically recite that x and x' in formula VI are CR11 and CR15, respectively (*i.e.* are not N as required by the compound shown above), or recite specific compounds that do not include the compound shown above.

Regarding claims 21, 22, 24 and 27, solely in order to expedite prosecution of the instant application, Applicants have amended independent claim 21, currently on file, to remove "N" from the choice of substituents defined for x and x'. Applicants note that the above-noted compound formed by the condensation of diketone IV and aldehyde (i) does not fall within the scope of amended claim 21. Applicants submit that the subject matter of amended claim 21 and claims dependent thereon, is thus novel over Dora and, therefore, respectfully request that the Examiner withdraw this rejection.

Rejection under 35 U.S.C. §103

The Office Action has maintained the rejection of claims 21, 22, 24 to 27, 39 to 43 and 45 under 35 U.S.C. §103(a), alleging that these claims are unpatentable over Bannister *et al.*, WO 2000/78761 ("Bannister").

The Office Action stated that Applicants' arguments filed July 8, 2010, have been fully considered but are not found to be persuasive. In particular, in rejecting Applicants' arguments, the Office Action has attempted to distinguish the present case from the situations of Takeda and Eisai stating that:

> Bannister et al. teaches a generic set of compounds useful as antibacterials/antiinfectives which encompass the elected species of compound. One of ordinary skill in the art would therefore have the reasonable expectation that any and all compounds falling within the disclosed genus would be useful as antibacterials/antiinfectives. This was not the case in either *Takeda* or *Eisai*. The instant rejection is based on the fact that the prior art reference Bannister et al. discloses compounds of formula 1 (see page 18; also claims 1, 2 and 7-10 for a smaller subgenus of compounds). Bannister teaches several examples wherein R_2 is Me, X is NH, Y is N and R_1 is absent. Bannister fails to teach a specific embodiment wherein B is phenanthroline. . . . Again it is highlighted, that unlike in Takeda, the prior art reference at hand does not teach or suggest that such a substitution would be detrimental to the resulting activity of the compound.
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> Office Action mailed October 29, 2010, at pages 10-11.

With respect to Applicants' statement that a meaningful success in the context of the presently claimed invention must take account of the established purpose of the compounds as anti-cancer agents, which is neither taught nor suggested by Bannister, the Office Action stated that:

> [T]he fact that the prior art suggests a different utility for the claimed compounds/compositions is immaterial as the claims do not even recite a future intended use. However, even if the claims did set for the future intended use as an anti-cancer agent, this ultimate intended use a compound must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In the instant situation, there is nothing from the disclosure of Bannister which would prevent the compounds taught therein from being used as anti-cancer agents. In fact, page 3 of Bannister line 31 teaches that the disclosed compounds can be incorporated into pharmaceutical preparations to be administered for inhibiting the growth of bacterial microorganisms. In sum, the instant claims are directed to compounds which the teachings of Bannister make obvious.
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> *Id.* at 14.

Applicants respectfully traverse the Office Action's rejection and maintain for the reasons set forth in the response filed on July 8, 2010, that the Office Action has not set forth a *prima facie* case of obviousness. In further support of these arguments, Applicants respectfully

refer the Examiner to the "*2010 KSR Guidelines Update*" ("Guidelines") published in the Federal Register and, in particular, the discussion in the Guidelines of *Takeda*, as well as *In re Kubin,* 561 F.3d 1351 (Fed. Cir. 2009) and *Ortho-McNeil Pharmaceutical, Inc.* v. *Mylan Labs, Inc.,* 520 F.3d 1358 (Fed. Cir. 2008).

As noted in the Guidelines, in *In re Kubin*, the Federal Circuit outlined two classes of situations where "obvious to try" is erroneously equated with obviousness under §103, the first of which is: "[w]hen what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful" [emphasis added]. In this regard, Applicants again note that the number of possible permutations of Formula I as described in Bannister is enormous. Even if, as the Office Action maintains, the skilled worker were to consider the "smaller subgenus of compounds" encompassed by claims 1, 2 and 7 to 10 of Bannister, Applicants again reiterate from the arguments filed on November 6, 2009, that with respect to the substituents identified in this "smaller subgenus," the definition of "heterocyclyl" or "heterocylic group" includes more than 55 specifically named examples and also includes any and all 3- to 10-membered ring structures, whose structures include anywhere from 1 to 4 heteroatoms, and which may or may not be part of a polycycle (see page 11-12 of Bannister), and the definition of "aryl" (*i.e.* aromatic), which includes heteroaromatic, provides even more options for the "fused aromatic or heteroaromatic ring" (*i.e.* any and all 5-, 6- and 7-membered single-ring aromatic groups, which may include anywhere from 1 to 4 heteroatoms and which may be substituted at one or more positions and which further may include polycylic ring systems having between two and an undefined upper number of cyclic rings, in which only one of the rings need be aromatic) (see page 10 of Bannister). Thus, the number of possible permutations encompassed even by this "smaller subgenus" remains vast. Furthermore, there is nothing in Bannister that would lead the skilled worker to select the particular embodiments described in claims 1, 2 and 7 to 10, over the myriad specific embodiments contemplated by Bannister and described in the claims and at page 19, line 5, to page 33, line 13. With the possible exception of the specific examples, Bannister presents all embodiments as equally

worthy of consideration. Nowhere does Bannister provide any guidance as to which parameters were critical or which of the many possible choices is most likely to be successful.

Thus, while it is theoretically possible, as alleged by the Office Action, that each and every one of the many thousands of compounds encompassed by the various embodiments described in Bannister may exhibit some antibacterial/antiinfective activity, nothing in Bannister would suggest to the skilled worker that selection of a phenanthroline ring system in particular would be a preferred option. Applicants again remind the Examiner that Bannister fails to disclose any examples of compounds containing a phenanthroline ring system. Applicants assert that, in this case, as in *Takeda*, the art discloses "a broad selection of compounds any one of which could have been selected as a lead compound." Even though in *Takeda*, as noted by the Examiner, the "lead compound" identified in the art exhibited negative properties thus directing the skilled worker away from the compound, the Court was clear that "even if there had been reason to select compound b, there had been no predictability or reasonable expectation of success associated with the particular modifications necessary to transform compound b into the claimed compound pioglitazone" (see Guidelines at page 53654).

Again with respect to "reasonable expectation of success," Applicants respectfully submit that the Examiner's disregard of the intended use of the claimed compounds is erroneous. As noted in the Guidelines, in *Ortho-MacNeil*, it is clearly indicated that "whether a combination would predictably be effective for its intended purpose is part of the obviousness analysis" (see Guidelines at page 53654). In *Ortho-MacNeil*, as in the present case, the main claim at issue (claim 1) was directed to a compound. The intended use for the compound, which was not recited in the claim, was as an anti-convulsant. The prior art described compounds for anti-diabetic use. In its finding of non-obviousness, the Federal Circuit noted not only that there was no apparent reason why a person of ordinary skill would have chosen the particular starting compound or the particular synthetic pathway that led to the claimed compound as an intermediate, but also that there would have been no reason to test that intermediate for anticonvulsant properties if treating diabetes had been the goal. Thus, it is clear that the intended use of a compound that needs to be taken into consideration as a part of the obviousness enquiry is the use set forth in the specification and not the use described in the art. Accordingly, in the

context of the presently claimed compounds, a meaningful success must take account of the established purpose of the compounds (*i.e.* as anti-cancer agents). In the present case, there is no teaching or suggestion in the art that the compounds described in Bannister would have anti-cancer activity and the Office Action has not provided a reasoning why a skilled worker looking to develop an anti-cancer compound would start with an antibacterial/antiinfective.

In summary, therefore, Applicants maintain that the skilled worker looking to develop an anti-cancer compound would have no reason to start with the compounds described in Bannister. Furthermore, even if Bannister were used as a starting point, the skilled worker is not provided with any reason to select compounds having a phenanthroline ring system from amongst the multitude of options presented in Bannister and to modify these to provide the claimed compounds with a reasonable expectation of success, where success if defined by the intended use of the compounds described in the instant application (*i.e.* as anti-cancer agents).

In view of the foregoing, Applicants respectfully reiterate that the Office Action has not established a *prima facie* case of obviousness. Applicants thus maintain that the pending claims are not obvious in light of Bannister and therefore respectfully request that the Examiner withdraw this rejection.

Double Patenting

The Office Action has maintained the provisional obviousness-type double patenting rejection of claims 21, 22, 24 to 27, 39 to 43 and 45, alleging that these claims are unpatentable over claims 25, 26, 42, 43, 45, 74, 79, 81, 83, 87, 89, 91, 93, 95, 98 and 99 of copending Application No. 10/525,690 and over claims 43 to 74 of copending Application No. 11/915,257. The Applicants again respectfully request that these rejections be held in abeyance until an indication that the claims are otherwise allowable. Applicants, at that time, will either address these rejections or file a terminal disclaimer.

CONCLUSION

In light of the above amendments and remarks, the claims are believed to be allowable, and Applicants respectfully request notification of same. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of the application to issuance.

A three-month shortened statutory period was set for response, nominally ending January 29, 2011. Enclosed herewith is a Request for Three-Month Extension of Time, thereby extending the period for response to April 29, 2011. Therefore, this paper is timely.

Payment in the amount of $1,920.00 (reflecting the $810.00 fee for the Request for Continued Examination under 37 C.F.R. §1.17(e) and the $1,110.00 fee for the Request for Extension of Time under 37 C.F.R. §1.17(a)) is enclosed herewith. The payment is made electronically to be charged to a credit card. No further fee is believed due; however, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF EFS-WEB TRANSMISSION UNDER 37 C.F.R. § 1.8

I hereby certify that this correspondence – including any items indicated as attached, enclosed, or included – is being transmitted by EFS-WEB on the date indicated below.

/ D. Brian Shortell / April 28, 2011

D. Brian Shortell, JD, PhD Date